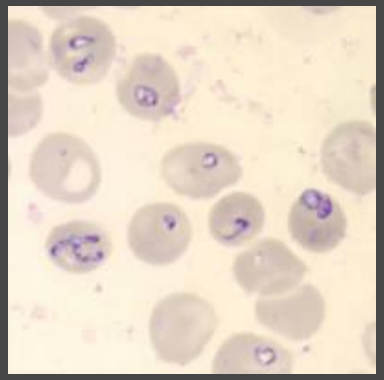
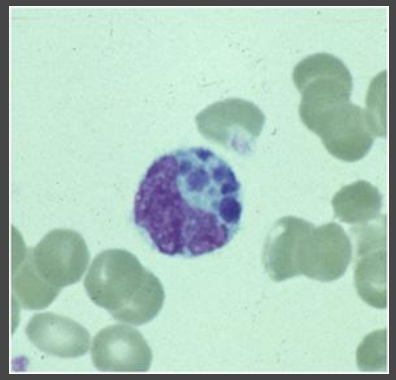
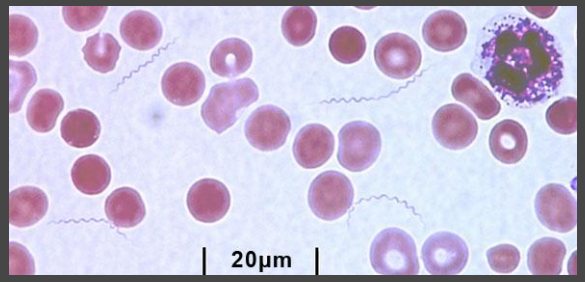
RECOGNIZING AND TREATING TICK-BORNE DISEASES



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Eastern Shore Health District

June 2013

Eastern Shore Community College, Melfa VA

Disclosures

- David Chang, M.D.
  - No Financial Interests or Relationships to Disclose

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Objectives

- By the end of this presentation, you will be able to:
  - Understand the complexity and difficulty of identifying and treating tick-borne diseases appropriately
  - Identify the 5 reportable tick-borne diseases
  - Identify 3 tick-borne diseases most likely to affect you and your family on the Eastern Shore
  - Recognize the basic signs and symptoms of the major tick-borne diseases
  - Understand some of the ongoing controversies in the field of tick-borne infections

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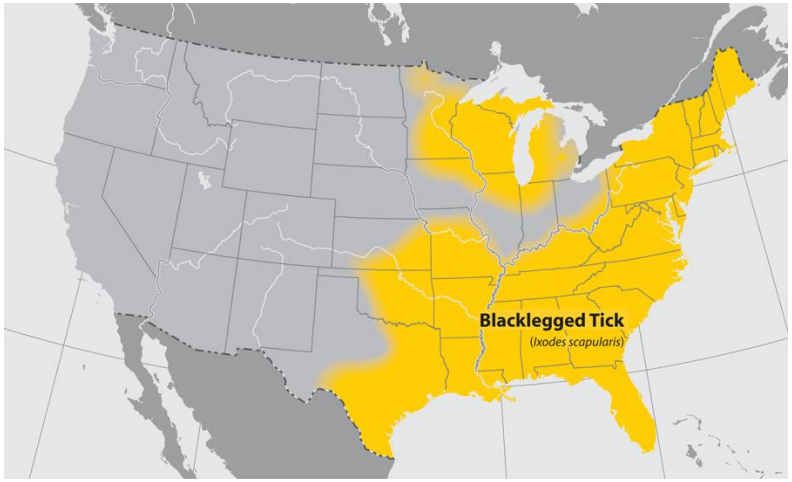
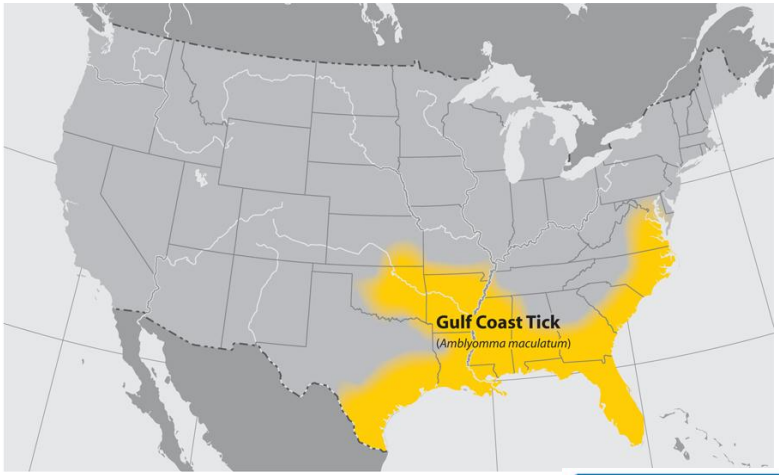
Geographic Distribution of Ticks





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Tick-Borne Diseases in US

- Anaplasmosis
- Babesiosis
- Ehrlichiosis
- Lyme Disease
- Ricketssia parkeri Ricketssiosis
- Rocky Mountain Spotted Fever (RMSF)
- Southern Tick-Associated Rash Illness (STARI)
- Tickborne relapsing fever (TBRF)
- Tularemia
- 364D Ricketssiosis - new disease in CA

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Tick-Borne Diseases Abroad

- Crimean-Congo hemorrhagic fever
- Other Ricketssial infections
- European Lyme Disease: Eastern Europe + Northern Asia, different species, different symptoms
- Tick-borne Encephalitis

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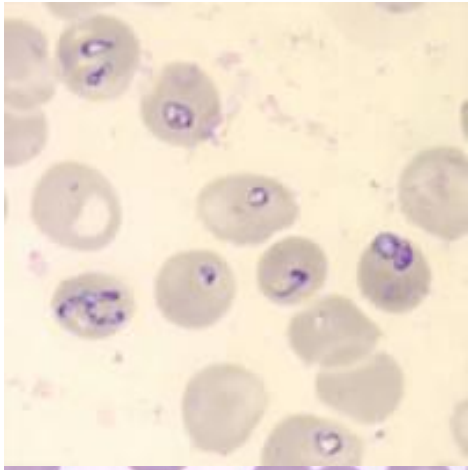
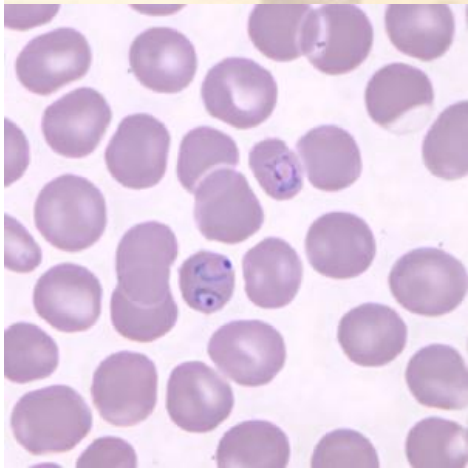
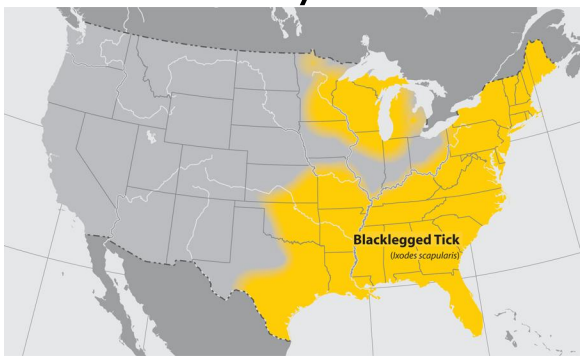
Babesiosis

- Caused by microsopic parasites that infect red blood cells
- Vector: black-legged ticks
- Symptoms: flu-like symptoms, often asymptomatic, but sometimes causes break down of blood cells (including red blood cells, platelets, and clotting factors), jaundice, dark urine
- Treatments: Atovaquone + Azithromycin or Clindamycin + Quinine x 7-10 Days
- Distribution:







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Other Ricketssial Diseases (not RMSF)

Ricketssia parkeri Ricketssiosis

- Vector: Gulf Coast Tick
- Distribution: E/S US along coast
- Symptoms: Fever, headache, eschar, rash
- Treatment: Doxycycline 100 mg BID x 7-14 d

364D Ricketssiosis

- Vector: Pacific Coast Tick
- Distribution: Northern CA
- Symptoms: Fever, Eschar
- Treatment: Doxycycline 100 mg BID x 7-14 D

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R. Parkerii Eschaar

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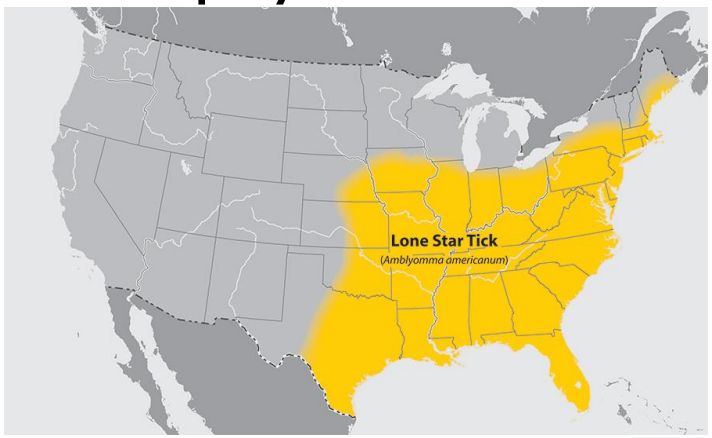
Southern Tick-Associated Rash Illness (STARI)

- Unknown cause
- Vector: Lone Star Tick
- Symptoms: Similar to Lyme Disease – bulls-eye lesion, flu-like symptoms
- Treatment: Unclear, but most physicians treat as LD
- Distribution: SE and E



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Distinctions between STARI & LD

STARI

- Patients recall tick bite
- Shorter onset of rash appearance (6v14 d)
- EM more circular and more central clearing
- Faster recovery with antibiotics

Lyme Disease

- Accompanying symptoms with erythema migrans (EM)
- More skin lesions, larger skin lesions (6-28 cm v 6-10 cm)

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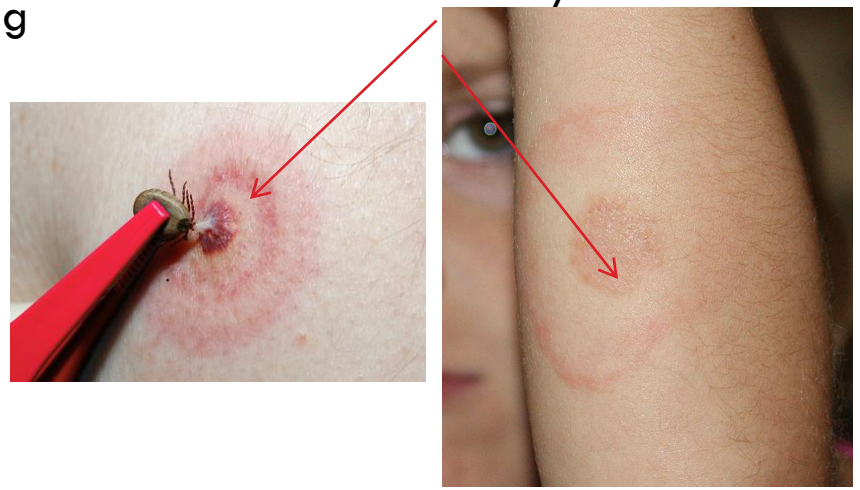
STARI vs LD

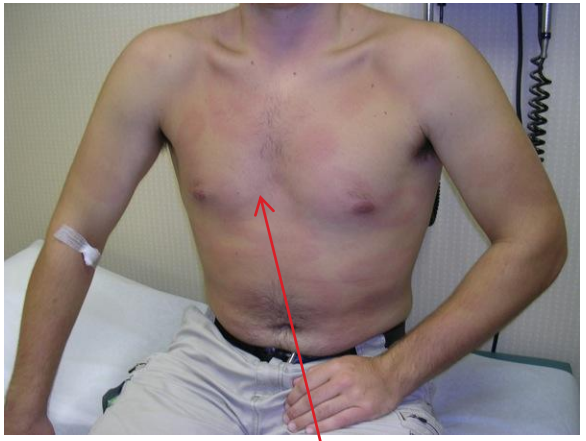
Circular

More Central Clearing

Smaller

Characteristic Bulls-Eye Rash





Multiple Skin Lesions

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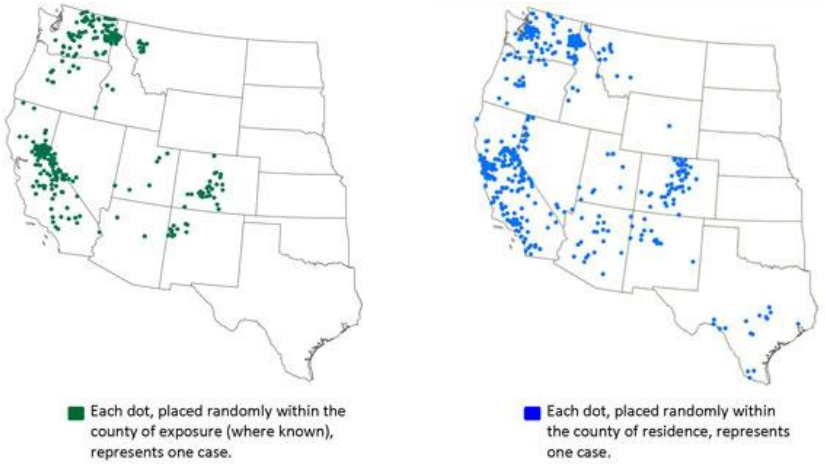
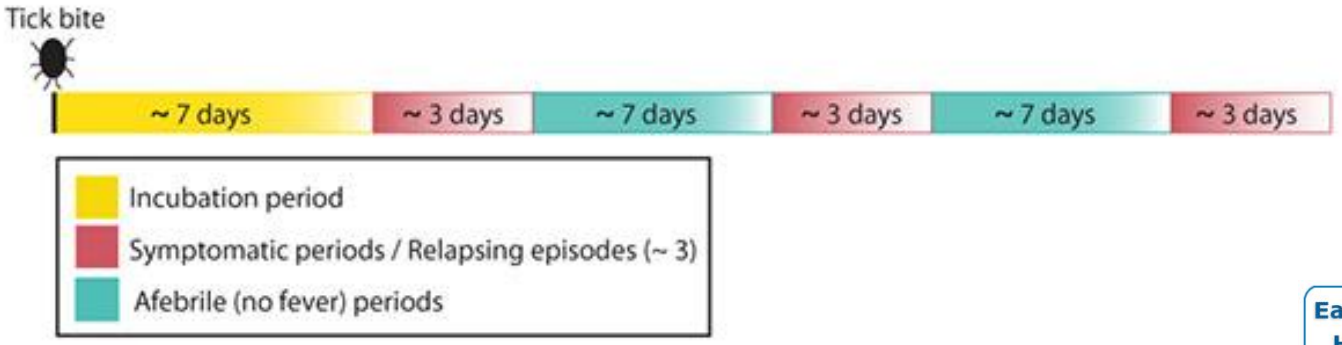
Tick-Borne Relapsing Fever (TBRF)

- Caused by bacterium Borrelia (several species)
- Vector: Soft Ticks
- Distribution
- High altitudes and caves
- Squirrels, owls, chipmunks
- Symptoms: relapsing fever, flu-like symptoms





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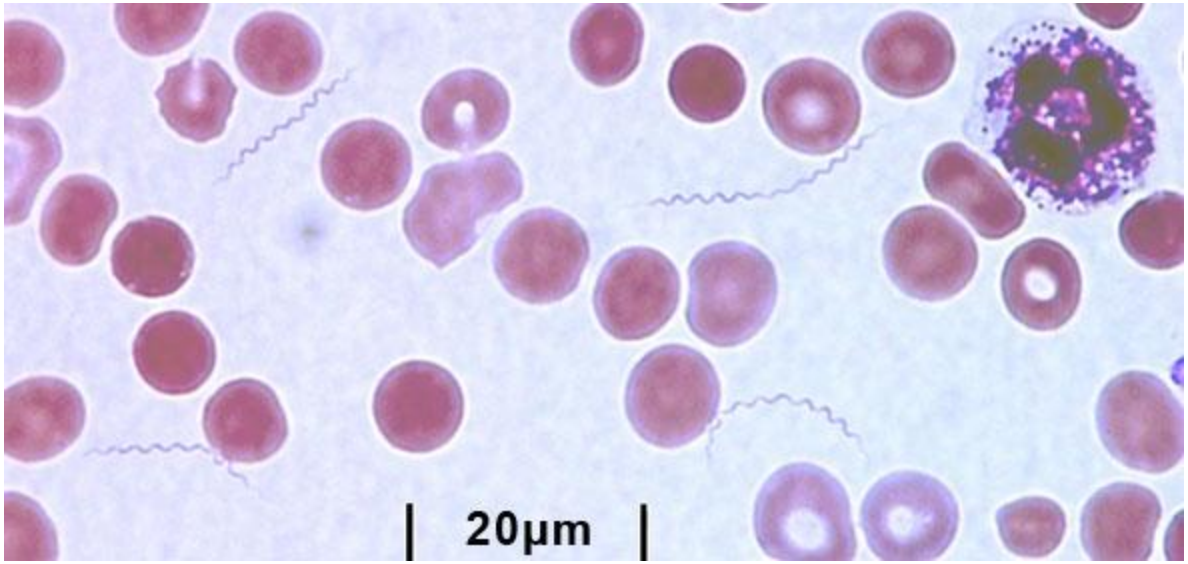
TBRF



Treatment: Tetracycline 500 mg QID x 10 D or Ceftriaxone 2 grams daily x 10-14 D

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Anaplasmosis/Ehrlichiosis

	Anaplasmosis	Ehrlichiosis
Cause:	▫ Anaplasma phagocytophilum	▫ Ehrlichia chaffeensis, E. Ewingii, E. muris-like
Vector:	▫ Black-legged & Deer ticks	▫ Lone star tick
Geography:	▫ Upper MW and NE	▫ SE and S Central
Symptoms:	▫ Fever, headache, chills, muscle aches	▫ Fever, headache, fatigue, and muscle aches
Diagnosis:	▫ PCR, A. phagocytophilum antigen, blood smear	▫ PCR, E. Chaffeensis antigen, blood smear
Treatment:	▫ Doxycyline 100 mg PO BID x 1-2 W	▫ Doxycyline 100 mg PO BID x 1-2 W

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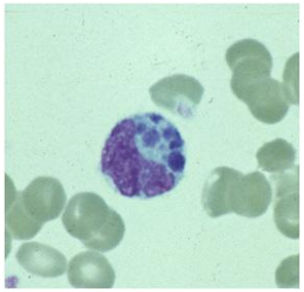
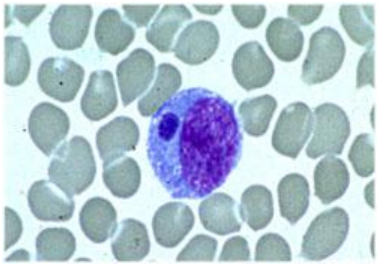
Anaplasmosis/Ehrlichiosis

	Anaplasmosis	Ehrlichiosis
Fatality Rate:	< 1%	1.8%
Rash:	None	60% children, 30% adults
Transfusions:	Risk through infected wbcs	Risk through infected wbcs
Delay:	1-2 weeks	1-2 weeks
Diagnosis:	Recent tick bites, exposure history, leukopenia and thrombocytopenia, elevated LFTs	Recent tick bites, exposure history, leukopenia and thrombocytopenia, elevated LFTs
Blood Smear:		

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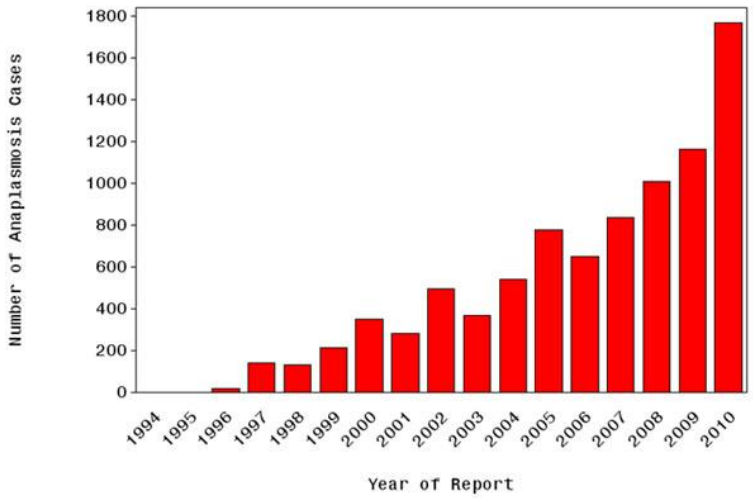
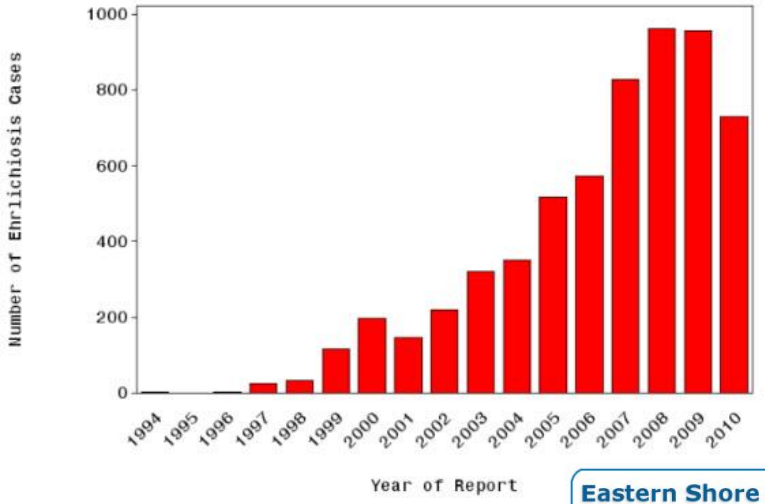
Anaplasmosis/Ehrlichiosis: Incidence

	Anaplasmosis	Ehrlichiosis
History:	◻ Recognized in 1990s, reportable in 1999	◻ Recognized in 1980s, reportable in 1999
Incidence:	◻ Rising	◻ Rising, plateaued in 2008

Number of Annual Anaplasmosis Cases, 1994-2010



Number of Annual Ehrlichiosis Cases, 1994-2010



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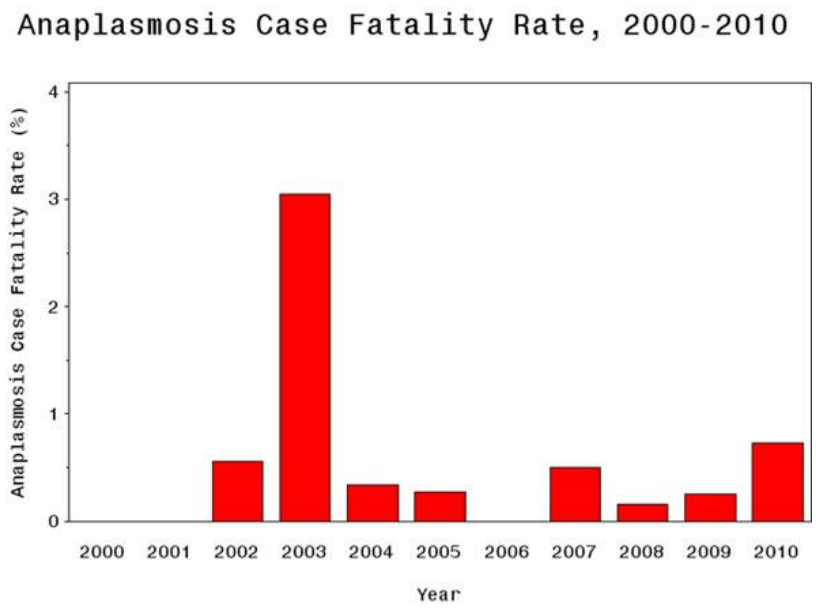
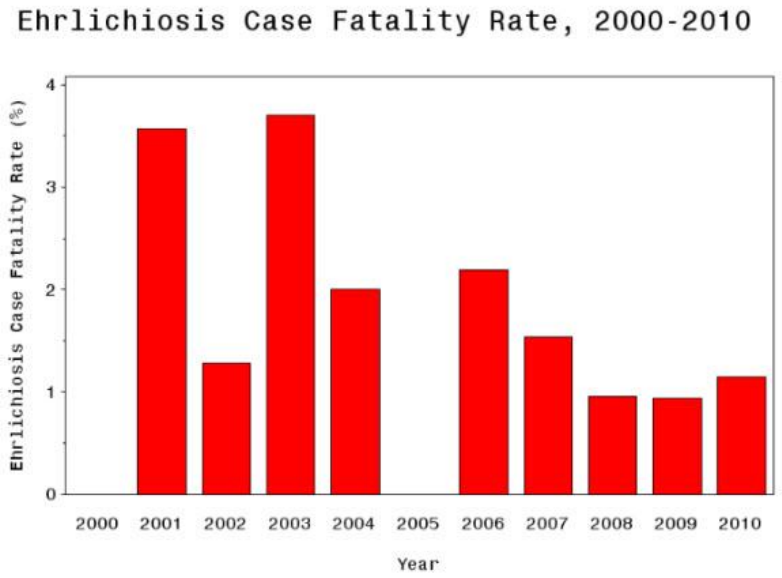
Anaplasmosis/Ehrlichiosis: Fatality

Anaplasmosis



Ehrlichiosis



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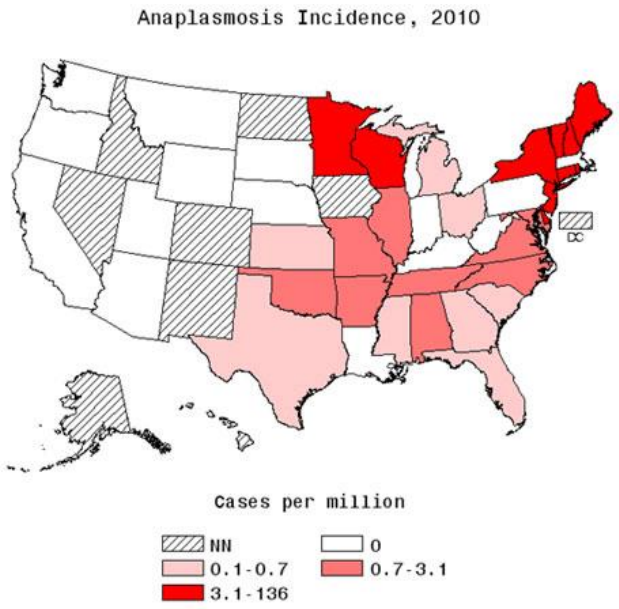
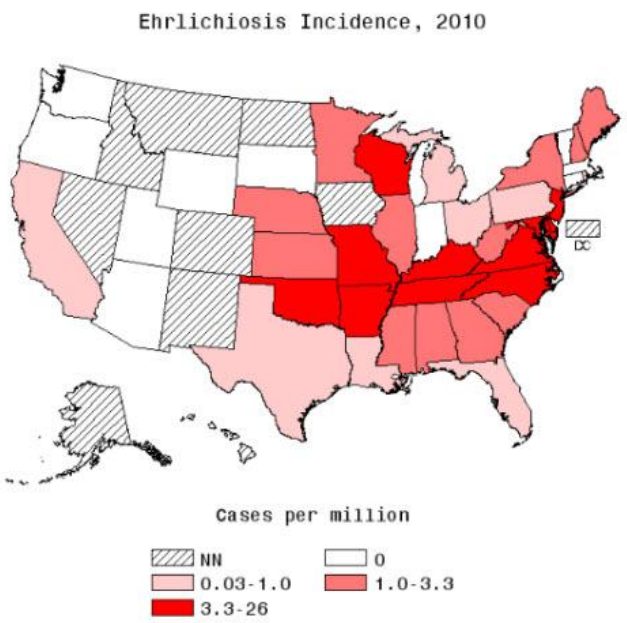
Anaplasmosis/Ehrlichiosis: Geography

Anaplasmosis



Ehrlichiosis



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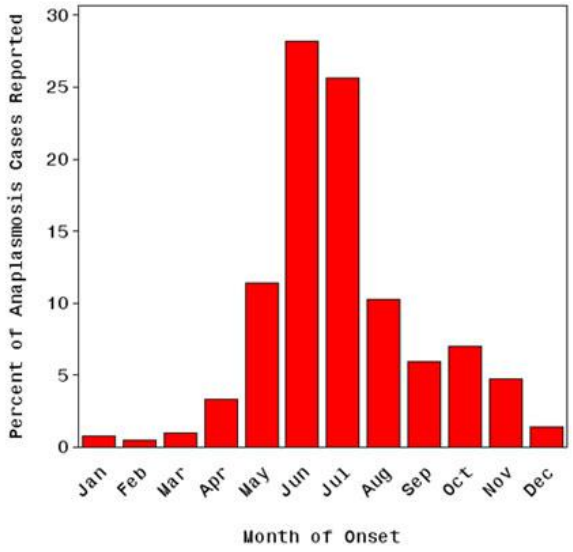
Anaplasmosis/Ehrlichiosis: Seasonality

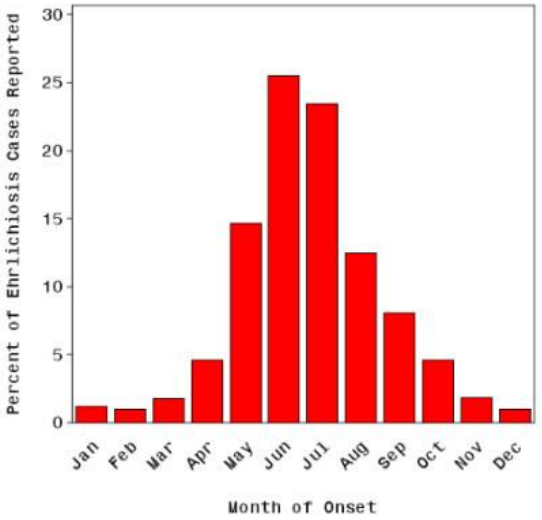
Anaplasmosis

Percent of Anaplasmosis Cases Reported each Month, 1994-2010



Ehrlichiosis

Percent of Ehrlichiosis Cases Reported each Month, 1994-2010



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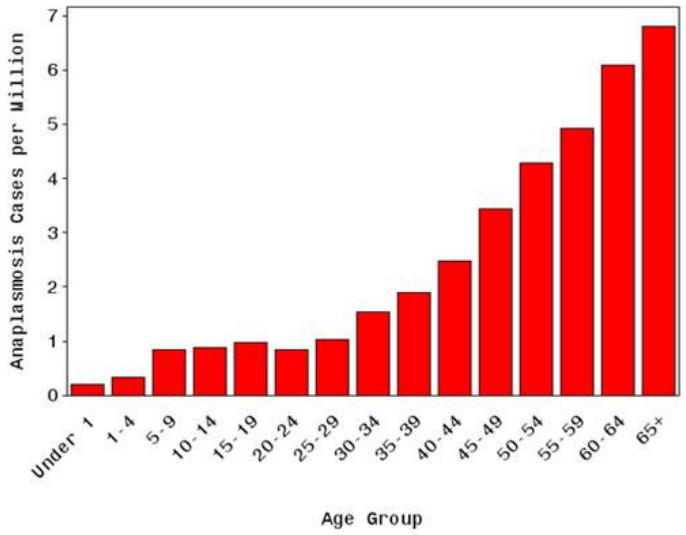
Anaplasmosis/Ehrlichiosis: Persons at Risk

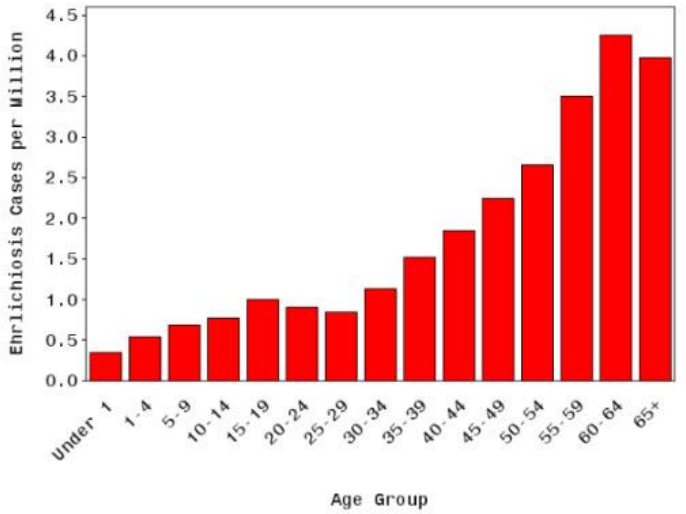
Anaplasmosis

Anaplasmosis Incidence by Age Group, 2000-2010



Ehrlichiosis

Ehrlichiosis Incidence by Age Group, 2000-2010



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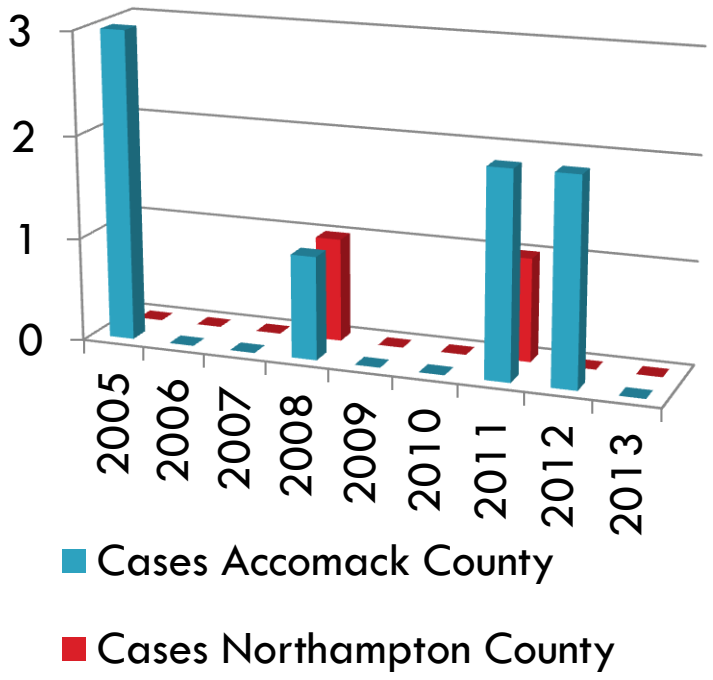
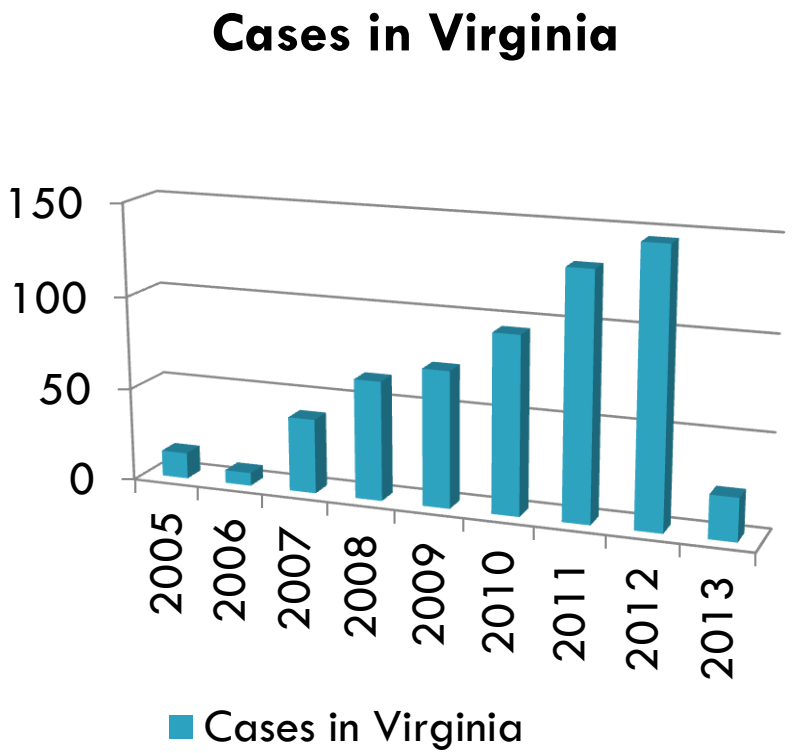
Anplasmosis/Ehrlichiosis Incidence on ES and VA

Eastern Shore Incidence



Virginia Incidence



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MMWR

Lyme Disease

- Cause: Bacterium Borrelia Burgdorferi
- Vector: Black-legged tick on E, NE, MW, & Western black-legged tick on Pacific Coast
- TRANSMISSION?:
  - Person-to-person contact
  - Maternal-child; breastmilk
  - Blood transfusion
  - Pets
  - Eating squirrel or venison meat
  - Air
  - Water
  - Bites of mosquitos, flies, fleas, or lice

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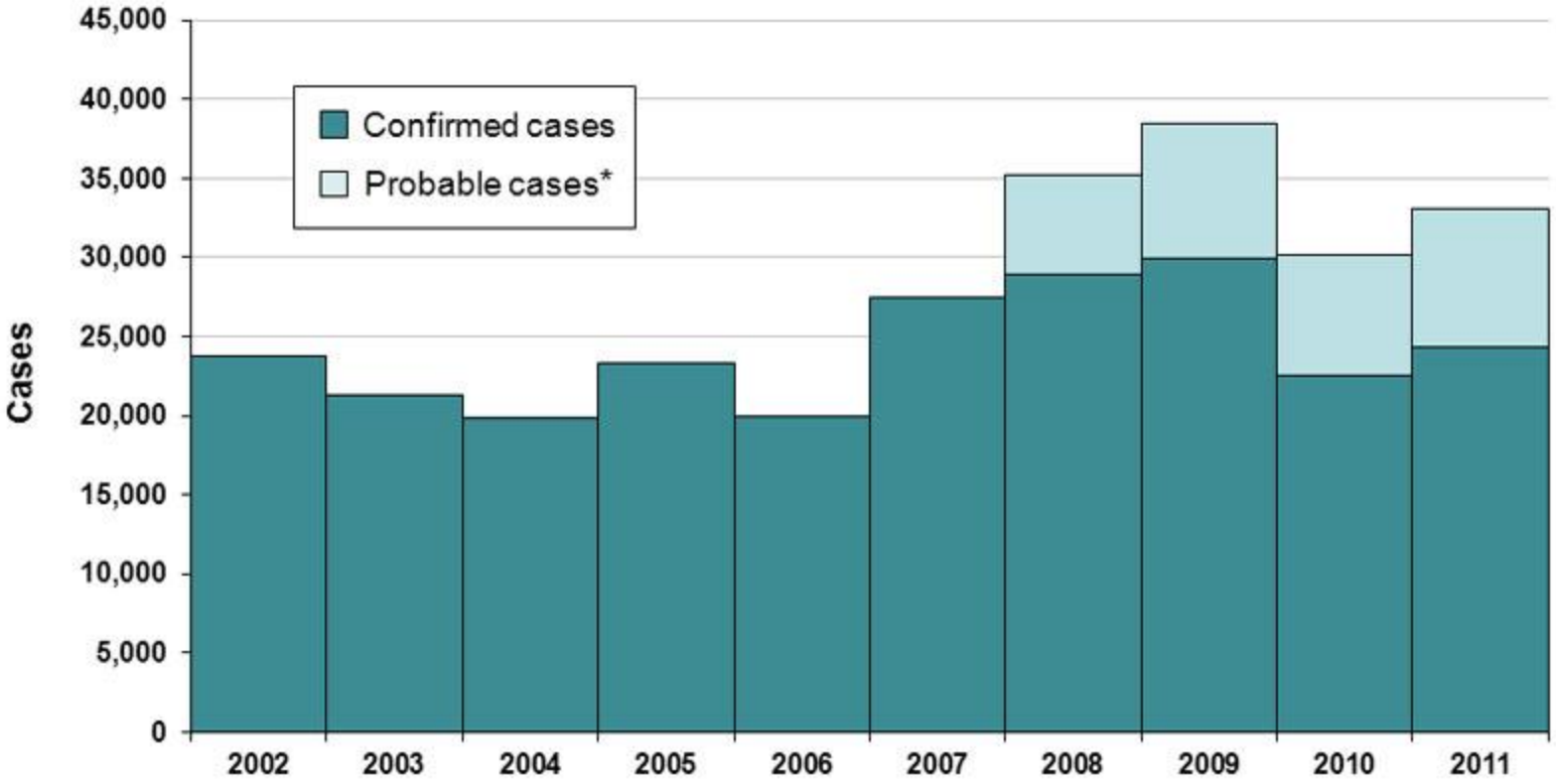
Lyme Disease: Incidence in US



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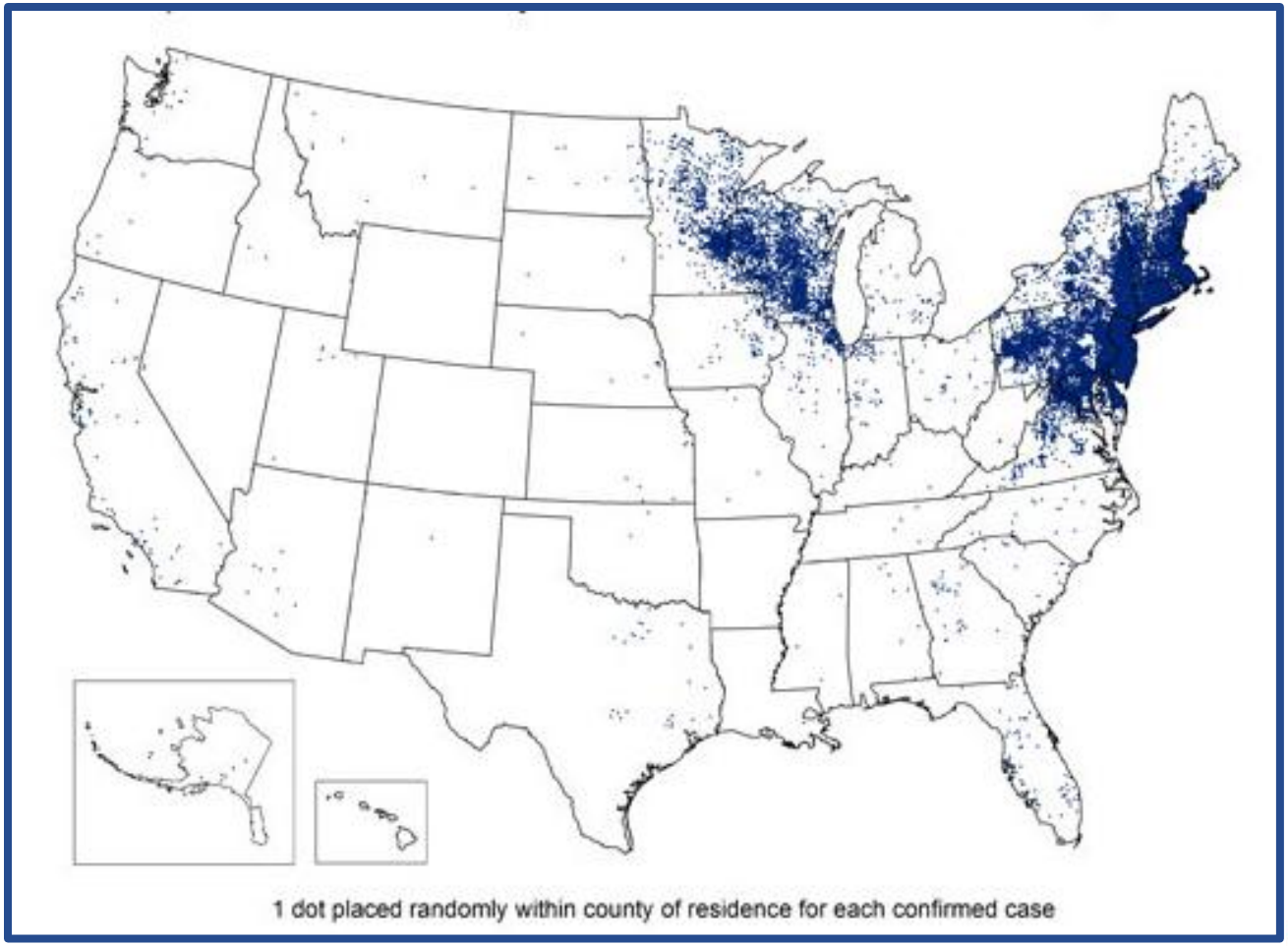
Lyme Disease: Geography



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Reportable Diseases: US 2010

Disease	Reported Cases
1. Chlamydia	1,307,893
2. Gonorrhea	309,341
3. Salmonellosis	54,424
4. Syphillis	45,834
5. HIV/AIDS	35,741
6. Lyme Disease	30,158
7. Pertussis	27,550
8. Giardiasis	19,811
9. Strep Pneumo	16,569
10. Varicella	15,427

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Reportable Diseases: Eastern Shore 2012

Disease	Reported Cases
1. Chlamydia	357
2. Gonorrhea	55
3. Salmonellosis	27
4. Campylobacter	11
5. Lyme Disease	9
6. Rocky Mountain Spotted Fever	8
7. HIV/AIDS	4
8. Elevated Lead Levels in Children	3
8. Pertussis	3
10. Tuberculosis	2

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Recognizing Lyme Disease

- Early Localized (3-30 days post-tick bite)
  - Flu-like symptoms
  - Red, expanding rash (Erythema Migrans)

- Early Disseminated (days to weeks)
  - Additional EM lesions
  - Facial Bell's Palsy
  - Meningitis
  - Arthritis
  - A-V Block

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Erythema Migrans

Typical, Early, Homegenous

Atypical, Late, Multiple

Dr. Michael Melia, June 2013 VDH Lyme Disease Presentation

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Late Disseminated & Post-Treatment Lyme Disease Syndrome

- 60% untreated progress to late disseminated
- Symptoms: intermittent bouts of arthritis, severe joint pain and swelling, chronic neurologic complaints

- Approximately 10-20% have symptoms after treatment
- Symptoms: joint and muscle pain, cognitive deficits, sleep disturbance, fatigue
- No evidence due to ongoing infection with B. burgdorferi (autoimmune)

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Diagnosis of Lyme Disease

- EM + Right Epidemiology = Lyme Disease
- NO NEED FOR LAB TESTING! TREAT.

- Typical LD symptoms + Lab Testing + EM History = Lyme Disease

- If uncertain, test during acute stage, and then test 4-6 weeks later (typically negative for first month)

- Atypical Symptoms + Wrong Epidemiology + No EM History + Positive Lyme IgG = Likely other cause of symptoms
- What to do in this case? Unclear, could treat or not treat.
- THUS, LAB TESTING SHOULD NOT BE DONE WHEN THERE IS A LOW INDEX OF SUSPICION FOR LYME.

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Lyme Disease Treatment Options

Drug	Dosage for adults	Dosage for children
Preferred oral regimens		
Amoxicillin	500 mg 3 times per day[a]	50 mg/kg per day in 3 divided doses (maximum, 500 mg per dose)[a]
Doxycycline	100 mg twice per day[b]	Not recommended for children aged <8 years
		For children aged ⩾8 years, 4 mg/kg per day in 2 divided doses (maximum, 100 mg per dose)
Cefuroxime axetil	500 mg twice per day	30 mg/kg per day in 2 divided doses (maximum, 500 mg per dose)
Alternative oral regimens		
Selected macrolides[c]	For recommended dosing regimens, see footnote *d* in table 3	For recommended dosing regimens, see footnote in table 3
Preferred parenteral regimen		
Ceftriaxone	2 g intravenously once per day	50–75 mg/kg intravenously per day in a single dose (maximum, 2 g)
Alternative parenteral regimens		
Cefotaxime	2 g intravenously every 8 h[d]	150–200 mg/kg per day intravenously in 3–4 divided doses (maximum, 6 g per day)[d]
Penicillin G	18–24 million U per day intravenously, divided every 4 h[d]	200,000–400,000 U/kg per day divided every 4 h[d] (not to exceed 18–24 million U per day)

[a] Although a higher dosage given twice per day might be equally as effective, in view of the absence of data on efficacy, twice-daily administration is not recommended.
[b] Tetracyclines are relatively contraindicated in pregnant or lactating women and in children <8 years of age.
[c] Because of their lower efficacy, macrolides are reserved for patients who are unable to take or who are intolerant of tetracyclines, penicillins, and cephalosporins.
[d] Dosage should be reduced for patients with impaired renal function.

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Wormser G P et al. Clin Infect Dis. 2006;43:1089-1134

Lyme Disease Treatment Duration

Indication	Treatment	Duration, days (range)
Tick bite in the United States	Doxycycline, 200 mg in a single dose[a,b]; (4 mg/kg in children ≥8 years of age) and/or observation	…
Erythema migrans	Oral regimen[c,d]	14 (14–21)[e]
Early neurologic disease		
Meningitis or radiculopathy	Parenteral regimen[c,f]	14 (10–28)
Cranial nerve palsy[a,g]	Oral regimen[c]	14 (14–21)
Cardiac disease	Oral regimen[a,c,h] or parenteral regimen[a,c,h]	14 (14–21)
Borrelial lymphocytoma	Oral regimen[c,d]	14 (14–21)
Late disease		
Arthritis without neurologic disease	Oral regimen[c]	28
Recurrent arthritis after oral regimen	Oral regimen[a,c] or parenteral regimen[a,c]	28 14 (14–28)
Antibiotic-refractory arthritis[i]	Symptomatic therapy[j]	…
Central or peripheral nervous system disease	Parenteral regimen[c]	14 (14–28)
Acrodermatitis chronica atrophicans	Oral regimen[c]	21 (14–28)
Post–Lyme disease syndrome	Consider and evaluate other potential causes of symptoms; if none is found, then administer symptomatic therapy[a]	…

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Wormser G P et al. Clin Infect Dis. 2006;43:1089-1134

Lyme Disease Antibiotics

- Lyme Disease is a bacteria. Antibiotics work.
  - 10-21 Days for Early Infections (Doxycyline)
  - 14-28 Days for Early Disseminated (Doxycyline or Ceftriaxone IV)
  - 2nd course of antibiotics almost never needed
  - However, with a longer duration of an untreated infection, most symptoms may persist after treatment (autoimmune)

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Lyme Disease Controversies

- Did the Doctor give me right diagnosis?
  - Diagnosis is almost always done without laboratory testing because early testing for PCR is 70% negative and bacteria are very difficult to identify in culture.
- How do I know I'm cured?
  - About 10-15% of people continue to have symptoms after adequate treatment with antibiotics.
  - There is no test for cure of Lyme Disease.
- If I test positive for B. Burgdorferi, does it mean I need to be treated for Lyme Disease?
  - Several false positive cases from an inaccurate test (IgM, IgG, EIA), and people can have LD-like symptoms with several other diseases.

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Lyme Information: Internet

TABLE 1. Summary of Lyme Disease Information Given by 19 Websites

	Tick Bites	LD Diagnosis	Serology	Other Tests	Chronic LD	Treatment	Pregnancy	Breast-feeding
www.acponline.org	A	A	A	A	A	A	A	—
www.aldf.com	A	A	A	A	A	A	—	—
www.cdc.gov	A	A	A	A	—	A	—	—
www.fda.gov	A	—	A	A	—	A	—	—
www.healingwell.com	A	A	A	A	—	A	—	—
www.hopkins-arthritis.com	A	A	A	A	A	A	—	—
www.igenex.com	I	I	I	I	I	I	—	I
www.ilads.org	—	I	I	—	I	I	—	I
www.intelihealth.com	A	A	A	A	A	A	A	—
www.kidshealth.org	A	A	A	—	A	A	A	—
www.lyme.org	I	A	A	I	I	I	I	I
www.lymealliance.org	A	I	I	I	I	I	A	—
www.lymedisease.org	I	A	I	I	I	A	I	—
www.lymediseaseassociation.org	I	I	I	I	I	I	I	I
www.lymediseaseinformation.com	A	—	—	—	—	A	—	—
www.lymeinfo.net	—	—	I	A	I	—	—	I
www.lymenet.org	—	I	I	—	I	I	I	I
www.lymesite.com	I	I	I	—	I	—	I	I
www.webmd.com	A	A	A	A	A	A	—	—

LD indicates Lyme disease; A, accurate; I, inaccurate; —, not discussed or found.

Cooper JD, Feder HM Jr. ,Pediatr Infect Dis J. 2004;12:1105

Slide taken from Dr. Michael Melia, June 2013 VDH Lyme Disease Presentation

Eastern Shore Health District

Rocky Mountain Spotted Fever (RMSF)

- Cause: Bacterium Rickettsia Rickettsii
- Vectors: American Dog Tick, Rocky Mountain Wood Tick, Brown Dog Tick
- Symptoms: fever, rash, headache
- Late rash appearance (90%)
- Starts wrists/forearms/ankles ➔ trunk, palm, soles

Eastern Shore Health District

Reportable Diseases: Eastern Shore 2012

Disease	Reported Cases
1. Chlamydia	357
2. Gonorrhea	55
3. Salmonellosis	27
4. Campylobacter	11
5. Lyme Disease	9
6. Rocky Mountain Spotted Fever	8
7. HIV/AIDS	4
8. Elevated Lead Levels in Children	3
8. Pertussis	3
10. Tuberculosis	2

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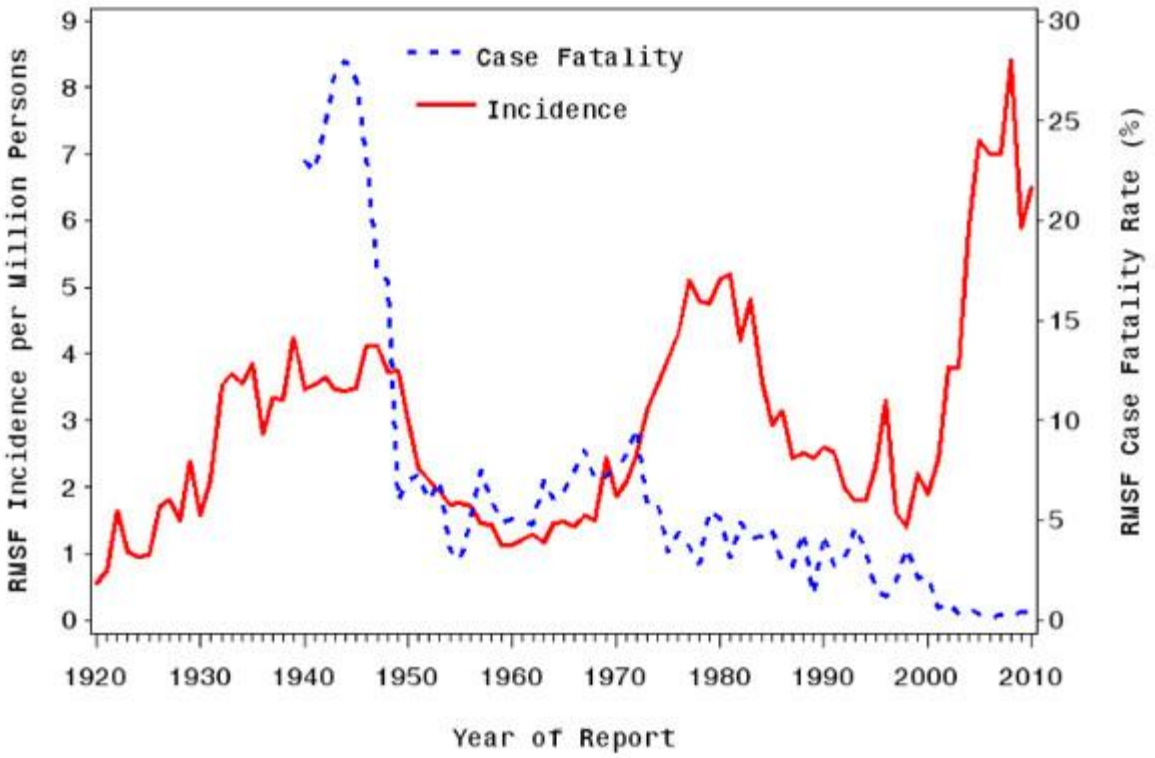
RMSF Incidence and Fatality



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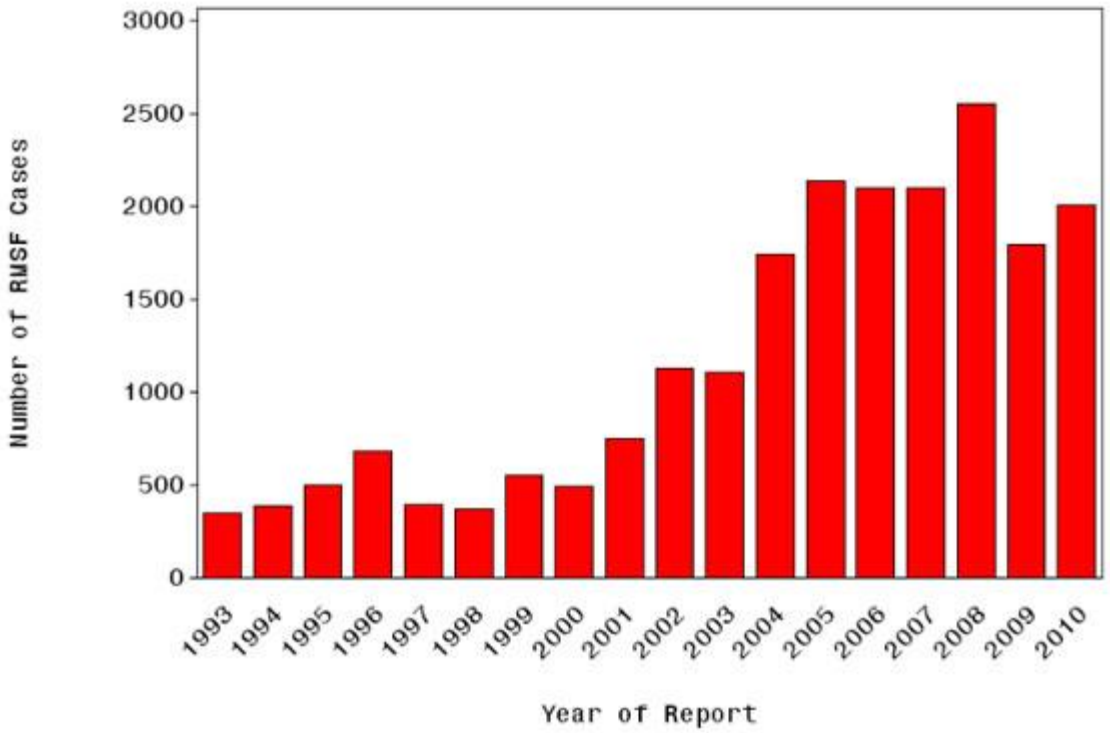
RMSF Incidence



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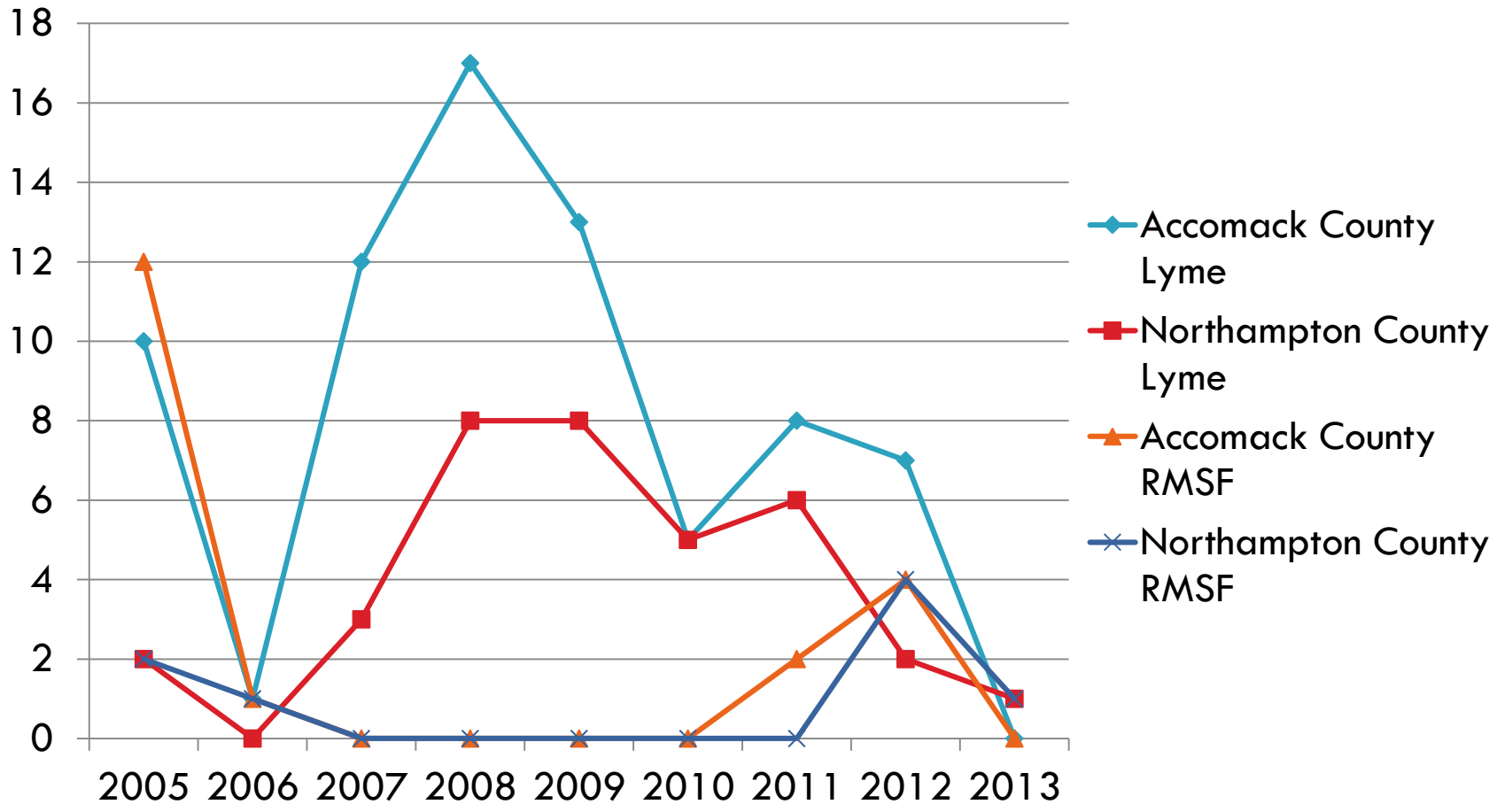
Lyme Disease vs RMSF Incidence on Eastern Shore



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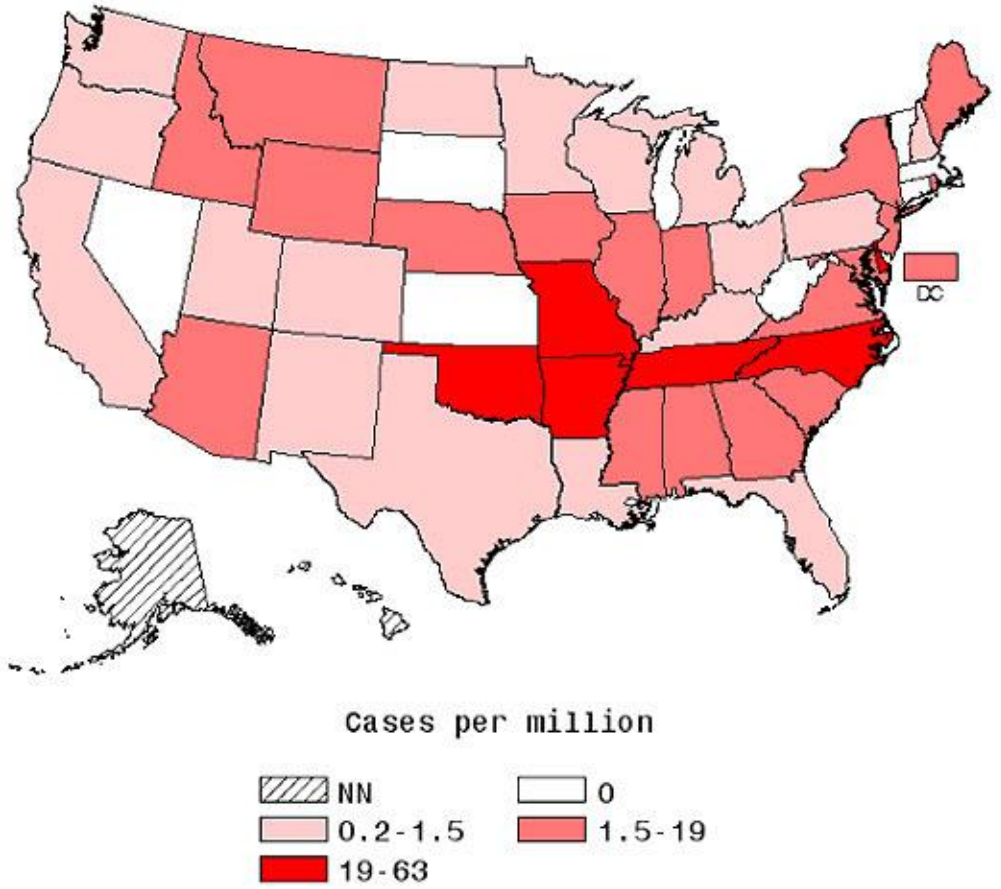
RMSF Geography



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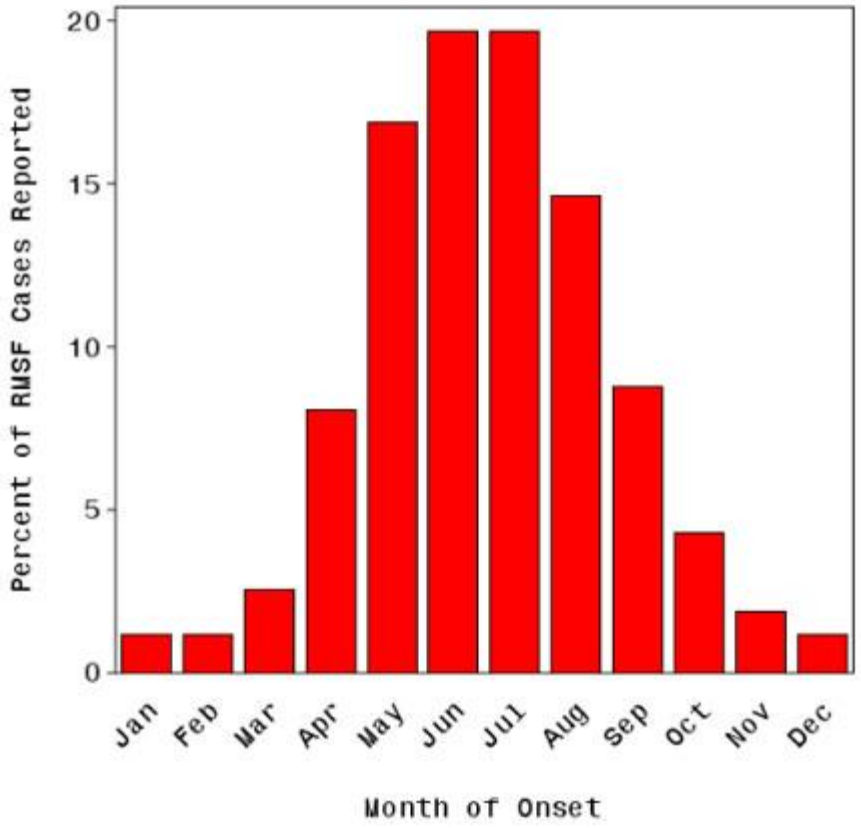
RMSF Seasonality: 1993-2010



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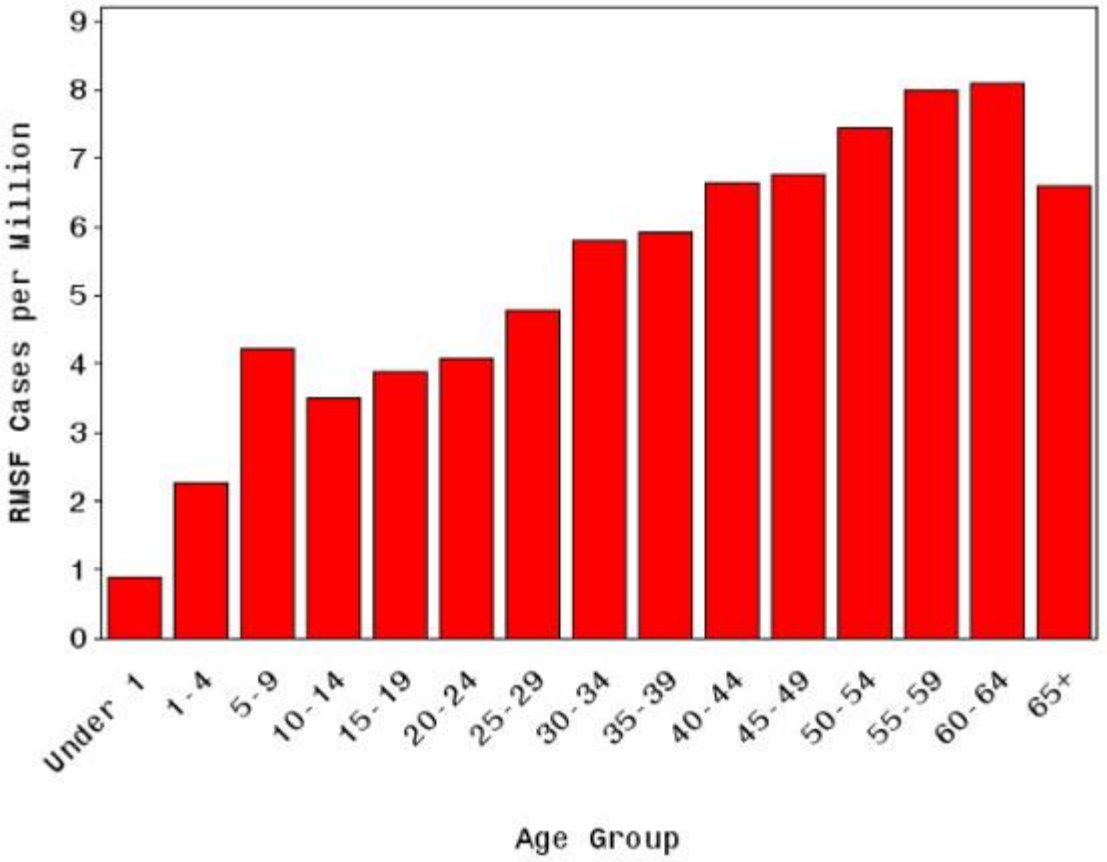
RMSF Persons at Risk: 2000-2010



RMSF Diagnosis

- Most difficult to diagnose of all the common tick-borne disease because:
  - Symptoms are variable
  - Symptoms are similar to other tick-borne disease
  - Detection of antibodies usually negative first 7-10 days
  - Rash appears late
  - Can be fatal if not treated within first 5 days
- Lab Findings: anemia, thrombocytopenia, hyponatremia, elevated LFTs
- Lab Confirmation: PCR (70% sensitivity), IFA antibodies

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RMSF Treatment

- Doxycyline 100 mg BID x 3 days after fever subsides or clinical improvement. Typically 7-14 days.
- Alternative: Chloramphenicol (pregnancy)

Eastern Shore Health District

Tularemia

- Cause: Bacterium Francisella tularensis
- Vectors: Ticks, Deer Flies, Skin Contact, Ingestion of Water, Lab Exposure, Inhalation of Aerosols
- Symptoms:
  - Ulcer at site of exposure + gland swelling (handling)
  - Glandular (bite)
  - Oculoglandular (eye)
  - Oropharyngeal (eating or drinking)
  - Pneumonic (inhalation)

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Tularemia Diagnosis and Treatment

- Diagnosis: epidemiologic link + symptoms + PCR/antibody titers
- Treatment: Streptomycin, Gentamicin, Doxycycline, or Ciprofloxacin x 10-21 days
- Almost all patients recovery completely

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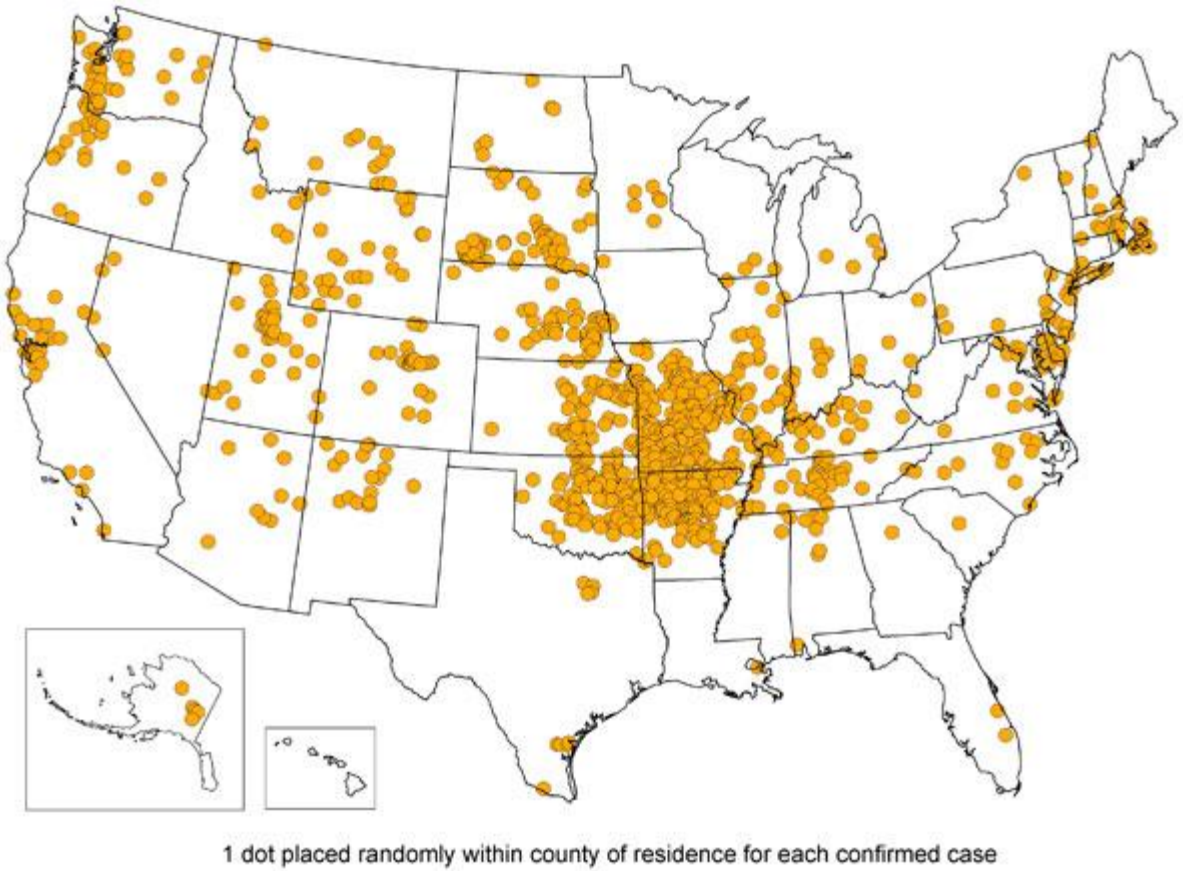
Tularemia Incidence 2001-2010



1 dot placed randomly within county of residence for each confirmed case

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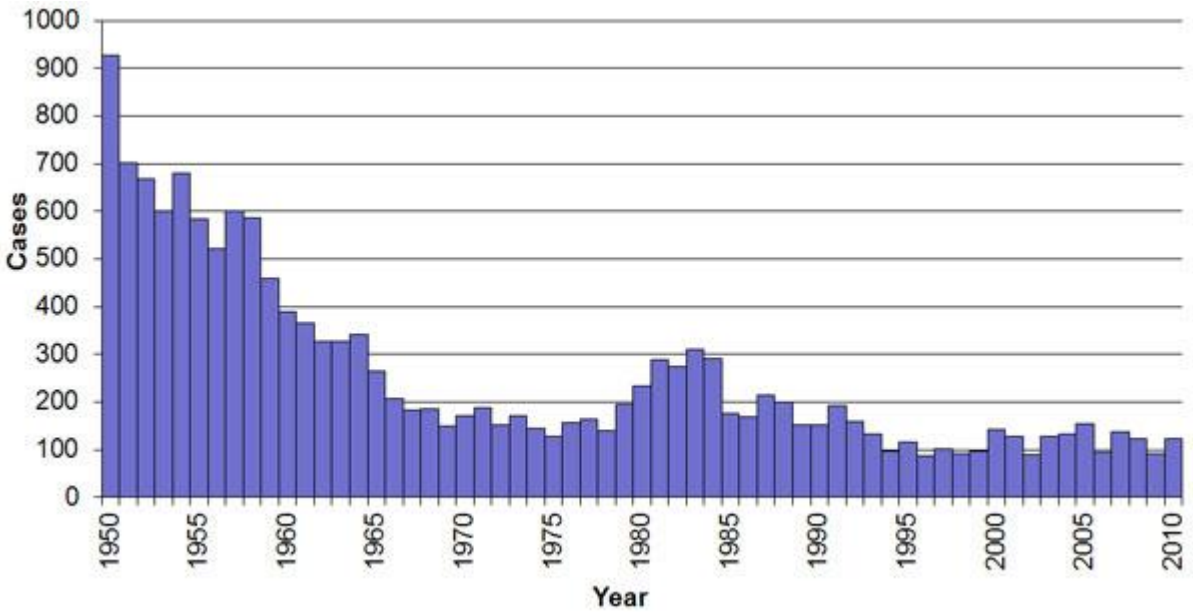
Tularemia Incidence



In Virginia, we have had 14 cases of Tularemia in past 10 years, 1 in this year.
On the Eastern Shore, we have had 1 case of Tularemia (Northampton County 2007.)

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www.cdc.gov

Special Considerations

- Nationwide shortage of Doxycycline since January 2013 due to increased demand and manufacturing issues
- Doxycycline should still be the only drug for prophylaxis of Lyme Disease
- Doxycycline should still be used to treat suspected ricketssial infections (RMSF, LD, Ehrlichiosis, Anaplasmosis); no other drugs have been proven to limit fatalities as effectively

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